

Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of the claims of the application:

Listing of Claims:

Claim 1 (currently amended): A dihydroxyalkylaminoalkyl- or dihydroxyalkylaminobenzyl-conjugated solid support, wherein the dihydroxyalkylamino moiety comprises the formula HO(CH₂)₂N(CH₂)₂OH, and wherein the solid support comprises a cross-linked polystyrene having about 1% to 2% cross-linking.

Claim 2 (currently amended): The solid support of claim 1, wherein the dihydroxyalkylaminoalkyl group or dihydroxyalkylaminobenzyl group is a diethanolaminomethyl, a diethanolaminoethyl, a diethanolaminopropyl, a diethanolaminobutyl group or a diethanolaminobenzyl group.

Claim 3: (Cancelled)

Claim 4 (currently amended): The solid support of claim 1, wherein the cross-linked polystyrene is comprises a cross-linked poly(styrene-divinylbenzene) (PS-DVB) copolymer having about 1% to 2% cross-linking.

Claims 5 to 12: (Cancelled)

Claims 13-15: (Cancelled)

Claim 16 (withdrawn): A method for making a solid support derivatized with a dihydroxyalkylamine group comprising mixing an aminoalkylated or aminobenzylated solid support comprising a primary amino group, with an excess of an epoxide, and a solvent, thereby derivatizing the solid support with a dihydroxyalkylamine group comprising a tertiary amine having two hydroxyalkyl substituents or two substituted hydroxyalkyl substituents.

Claim 17 (withdrawn): The method of claim 16, wherein the dihydroxyalkylamine group has the formula HO (CH₂)₂ N (CH₂)₂ OH.

Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 18 (withdrawn): The method of claim 16, wherein the dihydroxyalkylamine group has the formula $\text{HO}\text{CR}_2\text{CH}_2\text{NCH}_2\text{CR}_2\text{OH}$, and R is independently selected from the group consisting of H, $\text{C}_1\text{-C}_{20}$ alkyl radical, and $\text{C}_1\text{-C}_{20}$ substituted alkyl radical.

Claim 19 (withdrawn): The method of claim 16, wherein the mixing takes place under pressurized conditions in a sealed, pressure resistant container.

Claim 20 (withdrawn): The method of claim 16, wherein the epoxide comprises ethylene oxide, and the dihydroxyalkylamine group comprises a N,N -diethanolamine group.

Claim 21 (withdrawn): The method of claim 20, wherein the ethylene oxide in the sealed, pressure resistant container is a gas at about 1 to about 20 atmospheres.

Claim 22 (withdrawn): The method of claim 20, wherein the reaction takes place at about 50°C .

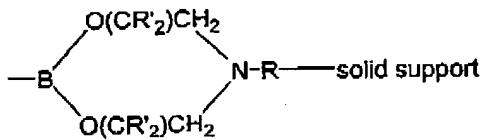
Claim 23 (withdrawn): The method of claim 16, wherein the epoxide comprises isobutylene oxide and the dihydroxyalkylamine group comprises a diisobutanolamine group.

Claim 24 (withdrawn): The method of claim 16, wherein the epoxide comprises an aryl-substituted oxirane.

Claim 25 (withdrawn): The method of claim 16, wherein the solvent comprises a tetrahydrofuran/water mixture or dioxane.

Claim 26 (withdrawn): The method of claim 16, wherein the mixing lasts for about 12 to 72 hours.

Claim 27 (withdrawn): A boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support, wherein the boronic ester-dioxyalkylamino group has a formula



Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

wherein R comprises an alkyl or a benzyl group, and R' is selected from the group consisting of H, C₁-C₂₀ alkyl radical, and C₁-C₂₀ substituted alkyl radical.

Claim 28 (withdrawn): The boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 27, wherein the boronic ester is an aryl boronic ester, a vinylboronic ester or an alkylboronic ester.

Claim 29 (withdrawn): The boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 27, wherein the solid support is selected from the group consisting of:

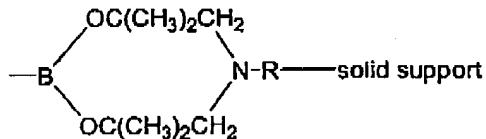
- i. a polystyrene or an equivalent composition;
- ii. a plastic or a plastic co-polymer;
- iii. a silica or a silica gel;
- iv. cellulose or cellulose acetate;
- v. a polyphenol, a polyvinyl, a polypropylene, a polyester, a polyethylene, a polyethylene glycol, a polystyrene-copolymer, or a co-polymeric mixture thereof;
- vi. a poly(vinyl alcohol) (PVA) hydrogel;
- vii. a polyacrylamide.

Claim 30 (withdrawn): The boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 29, wherein the polystyrene is a cross-linked poly(styrene-divinylbenzene) (PS-DVB) copolymer.

Claim 31 (withdrawn): The boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 30, wherein the cross-linked poly(styrene-divinylbenzene) (PS-DVB) copolymer is about 1% to 2% cross-linked.

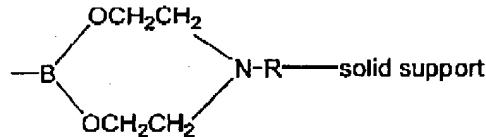
Claim 32 (withdrawn): The boronic ester-dioxyalkylaminoalkyl or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 27, wherein the boronic ester-dioxyalkylamino group has the formula

Appl. No. 09/943,465
 Amdt. Dated October 24, 2004 in Reply to Office Action
 dated January 29, 2004 and Non-Compliant Action dated September 24, 2004



wherein R comprises an alkyl or a benzyl group.

Claim 33 (withdrawn): The boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support of claim 27, wherein the boronic ester-dioxyalkylamino group has the formula

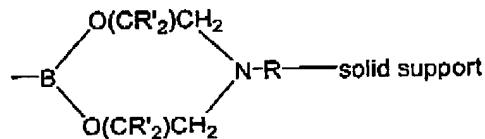


wherein R comprises an alkyl or a benzyl group.

Claim 34 (withdrawn): A method for making a boronic ester-dioxyalkylaminoalkyl- or boronic ester-dioxyalkylaminobenzyl-conjugated solid support comprising the following steps:

- (a) mixing an aminoalkylated or aminobenzylated solid support comprising a primary amino group, with an excess of an epoxide, and a solvent, thereby derivatizing the solid support with a dihydroxylalkylamine group comprising a tertiary amine having two hydroxyalkyl or two substituted hydroxyalkyl substituents;
- (b) mixing the dihydroxylalkylamine-derivatized solid support of step (a) with a boronic acid, in an anhydrous solvent, thereby derivatizing the solid support with a boronic ester-dioxyalkylaminoalkyl or dioxyalkylaminobenzyl group having the formula

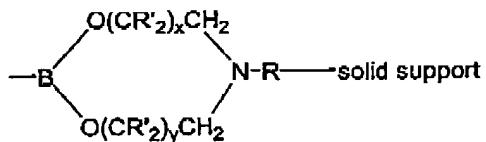
Appl. No. 09/943,465
 Amtd. Dated October 24, 2004 in Reply to Office Action
 dated January 29, 2004 and Non-Compliant Action dated September 24, 2004



wherein R comprises an alkyl or a benzyl group, and R' is selected from the group consisting of H, C₁-C₂₀ alkyl radical, and C₁-C₂₀ substituted alkyl radical.

Claim 35 (withdrawn): A method for immobilizing a boronic acid comprising the following steps:

- (a) providing a solid support derivatized with a dihydroxyalkylaminoalkyl group or a dihydroxyaminobenzyl group, wherein the dihydroxyalkylamino moiety has a formula HO (CR'2)_x CH₂N CH₂(CR'2)_y OH, wherein R' is independently selected from the group consisting of H, C₁-C₂₀ alkyl radical, and C₁-C₂₀ substituted alkyl radical, and x and y are integers between 1 to about 20,
- (b) providing a sample comprising at least one boronic acid; and
- (c) mixing the solid support of step (a) with the sample of step (b) in an anhydrous solvent, thereby immobilizing a boronic acid by generating a boronic ester-dioxyalkylaminoalkyl- or dioxyalkylaminobenzyl-conjugated group having the formula



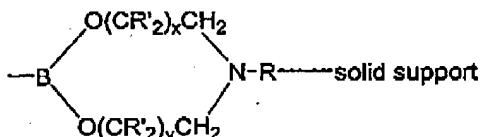
wherein R comprises an alkyl or a benzyl, R' comprises at least one of H and C₁-C₂₀ radical, and x and y are integers between 1 to about 20.

Claim 36 (withdrawn): A method for purifying a boronic acid comprising the following steps:

Appl. No. 09/943,465

Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

- (a) providing a solid support derivatized with a dihydroxyalkylaminoalkyl group or a dihydroxyaminobenzyl group, wherein the dihydroxyalkylamino moiety has a formula $\text{HO}(\text{CR}'_2)_x\text{CH}_2\text{NCH}_2(\text{CR}'_2)_y\text{OH}$, wherein R' is independently selected from the group consisting of H, $\text{C}_1\text{-C}_{20}$ alkyl radical, and $\text{C}_1\text{-C}_{20}$ substituted alkyl radical, and x and y are integers between 1 to about 20,
- (b) providing a sample comprising at least one boronic acid;
- (c) mixing the solid support of step (a) with the sample of step (b) in an anhydrous solvent, thereby immobilizing a boronic acid by generating a boronic ester-dioxyalkylaminoalkyl- or dioxyalkylaminobenzyl-conjugated group having the formula



wherein R comprises an alkyl or a benzyl, R' comprises at least one of H and $\text{C}_1\text{-C}_{20}$ radical, and x and y are integers between 1 to about 20; and

- (d) hydrolyzing the boronic ester linkage, thereby releasing from the support a purified boronic acid.

Claim 37 (withdrawn): The method of claim 36, wherein the hydrolyzing of step (d) is in a solution comprising tetrahydrofuran, water and acetic acid.

Claim 38 (withdrawn): The method of claim 36, wherein the hydrolyzing of step (d) is in a solution comprising tetrahydrofuran and water.

Claim 39 (withdrawn): The method of claim 36, further comprising washing the solid support at least once with an anhydrous solvent after the mixing of step (c) and before the hydrolysis of step (d).

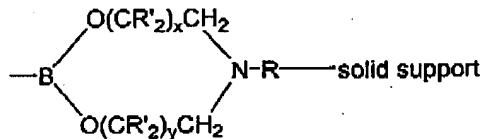
Claim 40 (withdrawn): The method of claim 36, performed in a batch or a column.

Appl. No. 09/943,465
 Andt. Dated October 24, 2004 in Reply to Office Action
 dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 41 (withdrawn): The method of claim 36, performed in an automated or semiautomated synthesizer.

Claim 42 (withdrawn): A method for scavenging a boronic acid from a multiple component solution to generate a boronic acid-free solution comprising the following steps:

- (a) providing a solid support derivatized with a dihydroxyalkylaminoalkyl group or a dihydroxyaminobenzyl group, wherein the dihydroxyalkylamino moiety has a formula $\text{HO}(\text{CR}'_2)_x\text{CH}_2\text{NCH}_2(\text{CR}'_2)_y\text{OH}$, wherein R' is independently selected from the group consisting of H , $\text{C}_1\text{-C}_{20}$ alkyl radical, and $\text{C}_1\text{-C}_{20}$ substituted alkyl radical, and x and y are integers between 1 to about 20,
- (b) providing a sample comprising at least one boronic acid;
- (c) mixing the solid support of step (a) with the sample of step (b), thereby immobilizing a boronic acid by generating a boronic ester-dioxyalkylaminoalkyl- or dioxyalkylaminobenzyl-conjugated group having the formula



wherein R comprises an alkyl or a benzyl, R' comprises at least one of H and $\text{C}_1\text{-C}_{20}$ radical, and x and y are integers between 1 to about 20; and

- (d) washing the solid support after the mixing of step (c) to remove non-boronic acid components; thereby scavenging the boronic acid from the multiple component sample to generate a boronic acid-free solution.

Claim 43 (withdrawn): The method of claim 42, wherein a molar excess of the support versus an estimated amount of boronic acid in the multiple component sample is used.

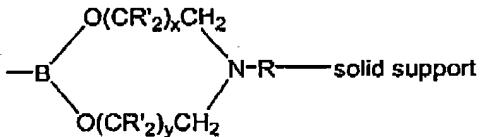
Appl. No. 09/943,465

Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 44 (withdrawn): A method for the solid phase synthesis of functionalized compounds comprising the following steps:

- (a) providing a boronic ester-dioxyalkylaminoalkyl or -dioxyalkylaminobenzyl-conjugated solid support,
- (b) providing a vinyl halide- or aryl halide- conjugated solid support;
- (c) providing a transfer agent;
- (d) combining the conjugated support of step (a) with the conjugated support of step (b) and the transfer agent of step (c) under conditions comprising a catalyst, a base and a solvent, thereby effecting coupling of the aryl or vinyl group of the conjugated support of step (a) with the vinyl or aryl group of step
- (e) to produce a solid supported, functionalized reaction product;
- (f) liberating the functionalized compound from the solid support.

Claim 45 (withdrawn): The method of claim 44, wherein the boronic ester-dioxyalkylaminoalkyl or -dioxyalkylaminobenzyl-conjugated solid support comprises the formula



wherein R comprises an alkyl or a benzyl, R' comprises at least one of H and C₁-C₂₀ radical, and x and y are integers between 1 to about 20.

Claim 46 (withdrawn): The method of claim 44, wherein the functionalized compound of step (e) is liberated from the solid support by reacting the solid supported reaction product of step (d) with a solvent comprising an acid and a non-protic, non-polar solvent.

Claim 47 (withdrawn): The method of claim 44, wherein the synthesized functionalized compound liberated from the solid support in step (e) comprises a functionalized biphenyl compound.

Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 48 (withdrawn): The method of claim 44, wherein the solid-supported boronic ester derivative originates from a poly-functionalized arylboronic acid containing at least one of the following substituents at at least one of the ortho-, meta- and para- positions:

- (a) a carboxamide;
- (b) a carboxylic ester;
- (c) a methylamino group;
- (d) an anilide group comprising an acyl group;
- (e) a urea comprising an acylamino group;
- (f) a sulfonamide comprising a sulfonyl group; or
- (g) an aryl alkyl ether.

Claim 49 (withdrawn): The method of claim 44, wherein the molar equivalent ratio of solid supported boronic ester of step (a) to the conjugated solid support of step (b) is about 3 to about 4.

Claim 50 (withdrawn): The method of claim 44, wherein the solid support comprises a polystyrene resin.

Claim 51 (withdrawn): The method of claim 44, wherein the solid-supported aryl halide of step (b) is a solid-supported polysubstituted halobenzoic acid, a solid-supported amino-substituted haloarene or a solid-supported aminoalkyl-substituted haloarene.

Claim 52 (withdrawn): The method of claim 44, wherein the catalyst of step (d) comprises a Pd(0) catalyst or a Pd(II) pre-catalyst.

Claim 53 (withdrawn): The method of claim 44, wherein the Pd(0) catalyst comprises a Pd(PPh₃)₄ or a Pd₂(dba)₃.

Claim 54 (withdrawn): The method of claim 44, wherein the solvent of step (d) comprises an aqueous solvent.

Appl. No. 09/943,465
Andt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 55 (withdrawn): The method of claim 44, wherein the transfer agent of step (c) comprises an aqueous solvent.

Claim 56 (withdrawn): The method of claim 44, wherein the base of step (d) comprises sodium carbonate, a trialkylamine, potassium fluoride, sodium fluoride or cesium fluoride.

Claim 57 (withdrawn): The method of claim 44, wherein the reaction conditions of step (d) comprise a temperature of between about 25°C to about 120°C.

Claim 58 (withdrawn): The method of claim 44, wherein the reaction conditions of step (c) comprise a reaction time of between about 1 hours to about 72 hours.

Claim 59 (withdrawn): The method of claim 44, wherein the solvent of step (d) comprises an anhydrous basic solvent.

Claim 60 (withdrawn): The method of claim 59, wherein the solvent of step (d) further comprises ethylene glycol as a co-solvent.

Claim 61 (withdrawn): The method of claim 59, wherein the solvent of step (d) comprises at least one tertiary amine base.

Claim 62 (withdrawn): The method of claim 59, wherein the reaction conditions of step (d) comprise a temperature of between about 25°C to about 120°C.

Claim 63 (withdrawn): The method of claim 44, wherein the reaction takes place in semiautomated parallel synthesizer.

Claim 64 (withdrawn): A semiautomated parallel synthesizer comprising

- (a) a boronic ester-dioxyalkylaminoalkyl or -dioxyalkylaminobenzyl-conjugated solid support, and
- (b) a vinyl halide- or aryl halide-conjugated solid support.

Claim 65 (withdrawn): A method for the solid phase synthesis of functionalized compounds comprising the following steps:

Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

- (a) providing a first reactant comprising a boronic ester-dioxyalkylaminoalkyl- or -dioxyalkylaminobenzyl- conjugated solid support;
- (b) providing a second reactant conjugated to a solid support;
- (c) providing a transfer agent;
- (d) providing a solvent
- (e) reacting the boronic ester-dioxyalkylaminoalkyl- or -dioxyalkylaminobenzyl- conjugated solid support of step (a) with the second reactant of step (b) and the transfer agent of step (c) in the solvent of step (d), thereby producing a solid supported, functionalized reaction product;
- (f) liberating the functionalized compound from the solid support.

Claim 66 (withdrawn): The method of claim 65, wherein the solvent of step (d) comprises an anhydrous solvent.

Claim 67 (withdrawn): The method of claim 65, wherein the solvent of step (d) comprises an aqueous solvent.

Claim 68 (withdrawn): The method of claim 67, wherein the transfer agent of step (c) comprises the solvent of step (d).

Claim 69 (withdrawn): The method of step 67, wherein the transfer agent of step (c) comprises water.

Claim 70 (withdrawn): The method of step 67, wherein the transfer agent of step (c) comprises an alcohol.

Claim 71 (withdrawn): A method for the solid phase synthesis of functionalized glycine compounds comprising the following steps:

- (a) providing a boronic ester-dioxyalkylaminoalkyl- or dioxyalkylaminobenzyl conjugated solid support;
- (b) providing a solid-supported iminium compound;
- (c) providing a transfer agent;

Appl. No. 09/943,465
Amtd. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

- (d) reacting the boronic ester-dioxyalkylaminoalkyl- or dioxyalkylaminobenzyl conjugated solid support of step (a) with the transfer agent of step (c) and the solid-supported iminium of step (b) in a solvent, thereby producing a solid supported, functionalized glycine reaction product; and,
- (e) liberating the functionalized compound from the solid support.

Claim 72 (withdrawn): The method of claim 71, wherein the solvent of step (d) comprises a hydroxylic solvent.

Claim 73 (withdrawn): The method of claim 71, wherein the hydroxylic solvent acts as the transfer agent of step (c).

Claim 74 (withdrawn): The method of claim 71, wherein reacting step (e) lasts for about 12 hours to about 48 hours.

Claim 75 (withdrawn): The method of claim 71, wherein the functionalized compound of step (e) is liberated from the solid support by reacting the solid supported reaction product of step (d) with a solvent comprising an acid and a non-protic, non-polar solvent.

Claim 76 (withdrawn): The method of claim 71, wherein step (d) further comprises the step of washing the solid supported, functionalized reaction product at least once with a solvent prior to liberating of the compound of step (e).

Claim 77 (withdrawn): A method for the solid-phase derivatization of a functionalized boronic acid comprising the following steps:

- (a) providing a dihydroxyalkylaminoalkyl or dihydroxyalkylaminobenzyl- conjugated solid support;
- (b) providing a sample comprising a functionalized boronic acid;
- (c) mixing the solid support with the sample in an anhydrous solvent, thereby immobilizing the functionalized boronic acid by generating a functionalized boronic ester-dioxyalkylaminoalkyl- or boronic dioxyalkylaminobenzyl-conjugated group;
- (d) providing at least one derivatizing agent capable of reacting with the functional group of the functionalized boronic acid; and

Appl. No. 09/943,465
Amdt. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

(e) contacting the derivatizing agent of step (d) with the functionalized boronic ester-dioxyalkylaminoalkyl- or functionalized boronic ester dioxyalkylaminobenzyl-conjugated group in a solvent, thereby producing a solid supported, derivatized boronic acid product.

Claim 78: (cancelled)

Claim 79 (withdrawn): The method of claim 77, further comprising reacting the solid supported, derivatized boronic acid with a solvent, thereby liberating the derivatized boronic acid from the solid support.

Claim 80 (withdrawn): The method of claim 77, wherein the functionalized boronic acid of step (b) comprises a formyl-functionalized benzeneboronic acid, and the derivatizing agent of step (d) comprises a primary or secondary amine, along with sodium borohydride.

Claim 81 (withdrawn): The method of claim 77, wherein the functionalized boronic acid of step (b) comprises a bromomethyl-functionalized benzeneboronic acid, and the derivatizing agent of step (d) comprises a primary or secondary amine.

Claim 82 (withdrawn): The method of claim 77, further comprising a coupling agent, and wherein the functionalized boronic acid of step (b) comprises a carboxy-functionalized arylboronic acid, and the derivatizing agent of step (d) comprises an amine.

Claim 83 (withdrawn): The method of claim 77, wherein the functionalized boronic acid of step (b) comprises an amino-functionalized boronic acid, and the derivatizing agent of step (d) comprises a isocyanate.

Claim 84 (withdrawn): The method of claim 78, wherein step (e) further comprises the step of washing the solid supported, derivatized reaction product at least once with a solvent prior to liberating of the compound.

Claim 85: (Cancelled)

Claim 86 (new): The solid support of claim 1, wherein the solid support comprises a cross-linked poly(styrene-divinylbenzene) copolymer having about 1% cross-linking.

Appl. No. 09/943,465

Amtd. Dated October 24, 2004 in Reply to Office Action
dated January 29, 2004 and Non-Compliant Action dated September 24, 2004

Claim 87 (new): An N,N-diethanolaminomethyl-conjugated solid support, wherein the solid support comprises a cross-linked polystyrene having about 1% to 2% cross-linking.

Claim 88 (new): The solid support of claim 87, wherein the solid support comprises a cross-linked poly(styrene-divinylbenzene) copolymer having about 1% to 2% cross-linking.

Claim 89 (new): The solid support of claim 88, wherein the solid support comprises a cross-linked poly(styrene-divinylbenzene) copolymer having about 1% cross-linking.